REMARKS

In view of the following remarks, the Examiner is requested to allow Claims 1, 5, 6 and 18-23, and new Claims 32-38, the only claims pending and under examination in this application.

The paragraph starting on page 5, line 5 is amended to insert the application serial number of the priority application. The paragraph starting on page 38, line 25 is amended to delete the blank space.

Cancel Claims 24-31. New Claims 32-38 are added. Support for the new claims is found in the specification, for example, in page 8, lines 19-21 and page 9, lines 4-7.

As no new matter has been added by way of these amendments, entry thereof by the Examiner is respectfully requested.

Specification

In light of the amendment to the specification, Applicants respectfully request the Examiner to withdraw the objection to the specification.

Claim Rejections – 35 U.S.C. § 102

Claim 1 is rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hsuih et al. (*J. Clin. Microbiol.* 34(3):501-507, 1996).

According to the MPEP, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. See MPEP 2131.

Claim 1 is directed to a method of quantifying the amount of **a target nucleic acid of less than about 30 nt in length**.

Hsuih et al. disclose using two hemiprobes to detect a hepatitis C virus (HCV) RNA whereby the two hemiprobes bind to the HCV RNA and are ligated to each other (page 503, Fig. 1). The HCV RNA is the nucleic acid that is the target of detection for

the hemiprobes. The HCV RNA is about 9.6 kb in length; which means the HCV RNA is not less than about 30 nucleotides in length. Accordingly, Hsuih et al. do not disclose **a target nucleic acid of less than about 30 nt in length**.

The Examiner identifies the hemiprobes of Hsuih et al. as "two different oligonucleotides that are 30 nucleotides in length and adjacently complementary ... with the target HCV RNA sequence" (page 4). Applicants respectfully point out that the Examiner appears to erroneously construe these two hemiprobes of Hsuih et al. as **a target nucleic acid of less than about 30 nt in length**. As described above, the target nucleic acid in Hsiuh et al. is the HCV RNA and not the two hemiprobes.

In view of the foregoing reasons, since Hsuih et al. fail to disclose each and every element of Claim 1, Hsuih et al. do not anticipate Claim 1. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Claims 18-20 and 22 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Wenz et al. (U.S. Patent Application No. 2003/0119004).

According to the MPEP, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. See MPEP 2131.

Claim 18 is directed to a method of quantifying an **siRNA** in a sample. Claims 19, 20 and 22 depend from Claim 18.

Wenz et al. disclose a method for quantitating a target nucleic acid sequence in a sample by hybridizing two target-specific probes to the target nucleic sequence, ligating the probes, amplifying the ligated probes and detecting the amplification product (page 1, paragraphs [0005] to [0006]). Wenz et al. further discloses that the target nucleic acid sequence "encompasses both DNA and RNA" and that the target nucleic sequence "may be described as a single-stranded [and that] a double-stranded target nucleic acid molecule may also serve as a target nucleic acid sequence" (page 5, paragraph [0061]). However, Wenz et al. do not disclose an **siRNA**.

Regarding the definition of siRNAs, the specification teaches that: "Particular siRNA molecules of interest are small ribonucleic acid molecules ... that are present in duplex structures, e.g., **two distinct oligoribonucleotides hybridized to each other, or a single ribooligonucleotide that assumes a small hairpin formation to produce a duplex structure.**" (page 8, lines 28-32; emphasis added). As Wenz et al. do not teach small RNA molecules that are two distinct oligoribonucleotides hybridized to each other, or a single ribooligonucleotide that assumes a small hairpin formation to produce a duplex structure, Wenz et al. do not disclose an **siRNA**.

In view of the foregoing reasons, since Wenz et al. fail to disclose each and every element of Claim 18-20 and 22, Wenz et al. do not anticipate Claim 18-20 and 22. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Claim Rejections – 35 U.S.C. § 103

Claims 1, 5-6 and 18-23 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Hsuih et al. and Wenz et al. in further view of Eglen (U.S. Patent Application No. 2006/0105377) and Hannon (*Nature* 418:244-251, 2002). Applicants respectfully traverse this rejection.

According to the MPEP § 706.02 (j), to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Under 35 U.S.C. § 102(e), the entire disclosure of a U.S. patent application publication, having an earlier effective U.S. filing date can be relied on to reject the claims. *Sun Studs, Inc. v. ATA Equip. Leasing, Inc.*, 872 F.2d 978, 983, 10 USPQ2d 1338, 1342 (Fed. Cir. 1989). See MPEP § 2136.02 (I).

As described above, Hsuih et al. disclose using two hemiprobes to detect a hepatitis C virus (HCV) RNA wherby the two hemiprobes bind to the HCV RNA and are ligated to each other (page 503, Fig. 1), but do not disclose **a target nucleic acid of less than about 30 nt in length**. In addition, Hsuih et al. do not teach or suggest an **siRNA** or **shRNA**.

As described above, Wenz et al. disclose a method for quantitating a target nucleic acid sequence in a sample by hybridizing two target-specific probes to the target nucleic sequence, ligating the probes, amplifying the ligated probes and detecting the amplification product (page 1, paragraphs [0005] to [0006]), but do not disclose an **siRNA** or **shRNA**. In addition, Wenz et al. do not teach or suggest **a target nucleic acid of less than about 30 nt in length**. Wenz et al. provide no teaching regarding the size of the target nucleic acid sequence, except in the Example section where four examples of target nucleic acid sequences are provided: the cDNA of the COX6b, RPS4x, GAPDH and beta-actin genes (pages 23-24, Table 2). In each case the sequence of the cDNA, to be bound by the ligation probes, are between 77 and 85 nucleotides in length. Accordingly, Wenz et al. provide no teaching or suggestion of applying their method for quantitating a target nucleic acid sequence of less than about 30 nucleotides in length.

Elgen, filed December 7, 2005 (hereafter Elgen '05), claims priority as a continuation-in-part application of application Ser. No. 10/702,232, filed November 6, 2003 (hereafter Elgen '03). As Elgen '05 is filed after the filing date of the present application (March 11, 2004), any new subject matter added to Elgen '05, that does not have support in Elgen '03, is not prior art. Elgen '03 discloses a method of intracellularly monitoring a β-galactosidase fusion protein interaction with a protein of interest, wherein the expression of the protein of interest is inhibited using a double-stranded RNA to in order to determine the effect of the RNA on the expression of the protein of interest. Accordingly, Elgen '03 does not teach or suggest an **siRNA** or **shRNA**.

Hannon discloses that siRNA and shRNA can be used to manipulate gene expression experimentally (page 250, first col., 3d full paragraph). Hannon discloses

that siRNA are double-stranded RNAs of lengths of about 21-23 nucleotides in length (page 248, Fig. 4).

There is no motivation or suggestion to combine Hsuih et al. or Wenz et al. with the subject matter of Elgen '03

There is no motivation or suggestion to combine Hsuih et al. or Wenz et al. with the subject matter of Elgen '03. This is because Hsuih et al. and Wenz et al. discloses methods of detecting nucleic acid, such as the HCV RNA of Hsuih et al. and the target nucleic acid sequence of Wenz et al. However, Elgen '03 discloses a method to determine the effect of a double-stranded RNA on the expression of a protein of interest. These are different methods for determining different variables. Hsuih et al. and Wenz et al. have the goal have determining the amount of a nucleic acid; while, in contrast, Elgen '03 is determining the efficiency of the double-stranded RNA in inhibiting the expression of a protein of interest.

Accordingly, there is no motivation or suggestion to combine Hsuih et al. or Wenz et al. with the subject matter of Elgen '03.

There is no motivation or suggestion to combine Hsuih et al. or Wenz et al. with Hannon

There is no motivation or suggestion to combine Hsuih et al. or Wenz et al. with Hannon. This is because Hsuih et al. and Wenz et al. discloses methods of detecting nucleic acid, such as the HCV RNA of Hsuih et al. and the target nucleic acid sequence of Wenz et al., which are many kilobases in length. However, Hannon discloses that siRNA are double-stranded RNAs of lengths of about 21-23 nucleotides in length. The HCV RNA and the nucleic acid sequences of Hsuih et al. and Wenz et al. are very distinct from the siRNA of Hannon, as the former are many kilobases in length and the latter are only about 21-23 nucleotides in length. The size difference is a more than 100-fold difference.

In addition, there is no reasonable expectation that applying the methods of Hsuih et al. and Wenz et al. would be successfully using the siRNA of Hannon of a potential target nucleic acid sequence. This region of binding for Hsuih et al. is 60 nucleotides in length and the regions of binding for Wenz et al. are 71-85 nucleotides in length. These binding regions are nearly at least 3 times the size of the siRNA of Hannon. There is no reasonable expectation that the method of Hsuih et al. and Wenz et al. would successfully work for the 21-23 nucleotide long siRNA of Hannon.

Accordingly, there is no motivation or suggestion to combine Hsuih et al. or Wenz et al. with the subject matter of Hannon.

Claims 1, 5 and 6 are not obvious.

Claim 1 is directed to a method of quantifying the amount of **a target nucleic acid of less than about 30 nt in length**. Claims 5 and 6 depend from Claim 1.

Claims 1, 5 and 6 are not obvious over Hsuih et al. and Wenz et al. in view of Elgen '03 and Hannon, because, for the reasons provided above, Hsuih et al. and Wenz et al. should not be combined with either Elgin '03 or Hannon. Accordingly, the deficiency of Hsuih et al. and Wenz et al. of not teaching or suggesting the element of **a target nucleic acid of less than about 30 nt in length** is not overcome. In addition, Elgen '03 and Hannon similarly do not teach or suggest any of the method steps of Claims 1, 5 and 6, and thus do not render the claims obvious.

Accordingly, a prima facie case of obvious is not established for Claims 1, 5 and 6 over the cited references.

Claims 18-23 are not obvious.

Claim 18 is directed to a method of quantifying an **siRNA** in a sample. Claims 19-23 depend from Claim 18.

Claims 18-23 are not obvious over Hsuih et al. and Wenz et al. in view of the Elgen '03 and Hannon, because, for the reasons provided above, Hsuih et al. and Wenz et al. should not be combined with either Elgin '03 or Hannon. Accordingly, the deficiency of Hsuih et al. and Wenz et al. of not teaching or suggesting the element of

an **siRNA** is not overcome. In addition, Elgen '03 and Hannon similarly do not teach or suggest any of the method steps of Claims 18-23, and thus do not render the claims obvious.

Accordingly, a prima facie case of obvious is not established for Claims 18-23 over the cited references.

Claims 5 and 6 are not obvious

Claims 5 and 6 contain the element an **siRNA**. As described above, Hsuih et al. and Wenz et al. do not teach or suggest the element "siRNA". Also, as described above, the subject matter of Elgen '03 does not teach or suggest the element "siRNA". For the reasons provided above, there is no motivation or suggestion to combine Hsuih et al. and Wenz et al. with Hannon.

Accordingly, a *prima facie* case of obvious is not established for Claims 5 and 6 over the cited references.

Claims 6 and 21 are not obvious

Claims 6 and 21 each contain the element **a shRNA**. As described above, Hsuih et al. and Wenz et al. do not teach or suggest the element "shRNA". Also, as described above, the subject matter of Elgen '03 does not teach or suggest the element "shRNA". For the reasons provided above, there is no motivation or suggestion to combine Hsuih et al. and Wenz et al. with Hannon.

Accordingly, a *prima facie* case of obvious is not established for Claims 6 and 21 over the cited references.

For the reasons provided above, the cited references do not render Claims 1, 5, 6 and 18-23 obvious. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

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CONCLUSION

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number NATH-003.

Respectfully submitted,
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Date: November 27, 2006

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